Ayala Pharmaceuticals Presents Positive Interim Data from Phase 2 ACCURACY Trial of AL101 for the treatment of Recurrent/Metastatic Adenoid Cystic Carcinoma with Notch Activating Mutations at ESMO 2020

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– Interim data showed meaningful clinical activity of AL101 4mg monotherapy with deep responses and 68% disease control rate

- Company to host virtual KOL event to review data today at 8:00am ET

REHOVOT, Israel and WILMINGTON, Del., Sept. 18, 2020 (GLOBE NEWSWIRE) -- Ayala Pharmaceuticals, Inc. (Nasdaq: AYLA) (Ayala or the Company), a clinical-stage oncology company focused on developing and commercializing small molecule therapeutics for patients suffering from rare and aggressive cancers, primarily in genetically defined patient populations, today announced positive interim results from the ongoing Phase 2 ACCURACY clinical trial of AL101 for the treatment of recurrent/metastatic (R/M) adenoid cystic carcinoma (ACC) harboring Notch-activating mutations in a mini oral presentation at the European Society for Medical Oncology (ESMO) Virtual Congress 2020.

“The study’s interim results are encouraging as we continue to study AL101 as a potential therapy for ACC patients with Notch-activating mutations. ACC is an orphan disease with no approved therapies and patients with Notch mutations have a more aggressive disease course and poorer survival outcomes as compared to patients with Notch wild-type,” said Renata Ferrarotto, M.D., Associate Professor, Department of Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center and principal investigator in the study. “It’s promising to see meaningful clinical activity, including a significant disease control rate with a single agent in this patient population that represents a major unmet clinical need.”

“We are pleased to see promising progress from the Phase 2 ACCURACY clinical trial of AL101 as a potential monotherapy for ACC with a significant disease control rate in the 4mg arm of 68% from 40 evaluable patients, building upon the 61% disease control rate from 27 patients that we reported in 2019,” said Roni Mamluk, Ph.D., Chief Executive Officer of Ayala. “Within the context of this difficult to treat cancer, in which people living with ACC have become accustomed to historically low response rates and failed therapies, it’s exciting to see signs of advancement with both safety and efficacy. We remain on track with enrollment in the 6mg dose cohort arm and we look forward to providing further trial progress updates in the first half of 2021.”

The ongoing Phase 2 ACCURACY clinical trial is an open-label, single-arm, multi-center study to assess the clinical activity of AL101 using radiographic assessments of patients with R/M ACC demonstrating disease progression within 6 months prior to dosing. The Company is evaluating the safety and efficacy of AL101 for the treatment of R/M ACC with Notch-activating mutations in two dose cohorts, 4mg once per week (QW) and 6mg QW. Dosing for the 6mg QW cohort commenced in March 2020 and is currently enrolling up to 42 subjects.

Updated Preliminary Safety and Efficacy Results:
As of July 30, 2020, of the 45 subjects who were enrolled in the 4 mg QW cohort, 40 were evaluable for efficacy for a best response by investigators using RECIST 1.1 criteria.

- Partial responses were observed in six subjects (15%) and stable disease was observed in 21 subjects (53%), yielding a 68% disease control rate;
- Approximately 40% of evaluable patients remained on drug for at least six months after entering the study with disease progression, including two patients treated beyond progression; and
- Pharmacokinetics (PK) results were similar to those of the AL101 Phase 1 study with no major effect by CYP inhibitors or substrates on AL101 exposure.

AL101 was generally observed to be well-tolerated, with most adverse events being mild to moderate in severity:

- Most treatment related adverse events (TRAEs) were of grade 1/2 severity; and
- The most common TRAEs of any grade included diarrhea (60%) of which 4% was grade 3, fatigue (51%) of which 4% was grade 3, nausea (49%) of which 2% was grade 3 and hypophosphatemia (42%) of which 4% was grade 3.

Virtual Key Opinion Leader (KOL) Conference Call and Webcast Event
Ayala will host a virtual event for investors and analysts to review the interim data from the Phase 2 ACCURACY clinical trial of AL101 for the treatment of R/M ACC. The live webcast event will begin at 8:00am ET and will include a discussion of the data with Alan L. Ho, M.D., Ph.D., Medical Oncologist at Memorial Sloan Kettering and a lead investigator of the ACCURACY clinical trial, as well as presentations from Ayala management.

To access the call, please dial 833-519-1339 (United States & Canada) or 914-800-3901(international) and reference the conference ID3995105. A live webcast of the conference call will be available on the Investors and News section of Ayala’s website at ir.ayalapharma.com. A replay of the webcast and accompanying slides will be available on the Ayala website for 90 days following the call.

About AL101
AL101 is an investigational small molecule, gamma secretase inhibitor that potently and selectively inhibits Notch 1, 2, 3 and 4. AL101 inhibits the

expression of Notch gene targets by blocking the final cleavage step by the gamma secretase required for Notch activation. It has the potential to inhibit tumor growth as demonstrated by three Phase 1 studies conducted by Bristol-Myers Squibb. AL101 is currently in a Phase 2 clinical trial in adenoid cystic carcinoma (ACC), as well as in a Phase 2 clinical trial for triple-negative breast cancer (TNBC) and planned Phase 2 clinical trial for T-Cell acute lymphoblastic leukemia (T-ALL).

About Adenoid Cystic Carcinoma (ACC)
ACC is a rare malignancy of the secretory glands including salivary glands, accounting for about 10% of all salivary gland tumors with an annual incidence of 3,400 in the U.S. There is currently no approved standard of care for patients with recurrent/metastatic ACC. Patients with locoregional disease undergo surgery and radiation therapy, with recurring disease treated by chemotherapy. ACC is an immunologically “cold” tumor that is refractory to chemotherapy, with a recurrence rate of about 60% after initial surgery. The Notch pathway has been determined to be an oncogenic driver of ACC and its dysregulation plays a key role in tumorigenesis and correlates with a distinct pattern of metastasis and a poor prognosis.

About the Notch Signaling Pathway
The Notch signaling pathway functions as a mediator of short-range cell to cell communication and plays a fundamental role in a variety of tissue types. The gain or loss of Notch signaling aspects has been associated with a wide range of disorders, developmental syndromes and cancers, both hematological and solid tumors. The Notch pathway is involved in several hallmarks of cancer including cellular proliferation, survival, migration, invasion, epithelial to mesenchymal transition and drug resistance, increased angiogenesis and metastasis.

About Ayala Pharmaceuticals
Ayala Pharmaceuticals, Inc. is a clinical-stage oncology company focused on developing and commercializing small molecule therapeutics for patients suffering from rare and aggressive cancers, primarily in genetically defined patient populations. Ayala’s approach is focused on predicating, identifying and addressing tumorigenic drivers of cancer through a combination of its bioinformatics platform and next-generation sequencing to deliver targeted therapies to underserved patient populations. The Company has two product candidates under development, AL101 and AL102, targeting the aberrant activation of the Notch pathway with gamma secretase inhibitors to treat a variety of tumors including Adenoid Cystic Carcinoma, Triple Negative Breast Cancer (TNBC), T-cell Acute Lymphoblastic Leukemia (T-ALL), Desmoid Tumors and Multiple Myeloma (MM) (in collaboration with Novartis). Ayala’s lead product candidate, AL101, has received Fast Track Designation and Orphan Drug Designation from the U.S. Food and Drug Administration and is currently in a Phase 2 clinical trial for patients with ACC (ACCURACY) bearing Notch-activating mutations and in a Phase 2 clinical trial for patients with TNBC (TENACITY) bearing Notch-activating mutations and other gene rearrangements. For more information, visit www.ayalapharma.com.

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Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements relating to our development of AL101, the promise and potential impact of our preclinical or clinical trial data, the timing of and plans to initiate additional clinical trials of AL101, upcoming milestones, including without limitation the timing and results of any clinical trials or readouts, and upcoming events and presentations. These forward-looking statements are based on management’s current expectations. The words “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “estimate,” “believe,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the impact of the COVID-19 pandemic on our operations, including our preclinical studies and clinical trials, and the continuity of our business; we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our cash runway; our limited operating history and the prospects for our future viability; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in regulatory approval; our requirement to pay significant payments under product candidate licenses; the approach we are taking to discover and develop product candidates and whether it will lead to marketable products; the expense, time-consuming nature and uncertainty of clinical trials; enrollment and retention of patients; potential side effects of our product candidates; our ability to develop or to collaborate with others to develop appropriate diagnostic tests; protection of our proprietary technology and the confidentiality of our trade secrets; potential lawsuits for, or claims of, infringement of third-party intellectual property or challenges to the ownership of our intellectual property; risks associated with international operations; our ability to retain key personnel and to manage our growth; the potential volatility of our common stock; costs and resources of operating as a public company; unfavorable or no analyst research or reports; and securities class action litigation against us. These and other important factors discussed under the caption “Risk Factors” in Quarterly Report on Form 10-Q for the six months ended June 30, 2020 filed with the U.S. Securities and Exchange Commission (SEC) on August 12, 2020 and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management’s estimates as of the date of this press release. New risk factors and uncertainties may emerge from time to time, and it is not possible to predict all risk factors and uncertainties. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.